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# THE EFFECT OF BEDREST ON VARIOUS PARAMETERS OF PHYSIOLOGICAL FUNCTION

## PART I. REVIEW OF THE LITERATURE ON THE PHYSIOLOGICAL EFFECTS OF IMMOBILIZATION

By C. Vallbona, F. B. Vogt, D. Cardus,
W. A. Spencer, and M. Walters



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ABSTRACT

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A review of literature (up to 1963) on the effects of immobilization reveals that bedrest has been evaluated in 83 subjects (30 of whom were allowed to sit up) and water immersion in 33 subjects. There is a wide variety of experimental conditions in each study. This precludes pooling of data to evaluate the significance of the findings. It is concluded that bedrest deserves further study with special attention to include: wider variety of subjects in regard to age, training habits, and physical condition; identification of physiological rhythms during bedrest; definition of changes in body composition; study of the mechanism of orthostatic hypotension following bedrest.

Author

# FOREWORD

This study is a part of a NASA investigation of the effect of bedrest on various parameters of physiological function. It was sponsored by NASA Manned Spacecraft Center under Contract NAS-9-1461, with Dr. Lawrence F. Dietlein, Chief, Space Medicine Branch serving as Technical Monitor.

This study was conducted in the Immobilization Study Unit of the Texas Institute for Rehabilitation and Research, The Texas Medical Center. The authors are affiliated with Baylor University College of Medicine as follows: Dr. Vallbona, Departments of Rehabilitation, Physiology, and Pediatrics; Dr. Vogt, Department of Rehabilitation; Dr. Cardus, Departments of Rehabilitation and Physiology; Dr. Spencer, Department of Rehabilitation; and Miss Walters, Research Dietitian, General Clinical Research Center for Chronic Illness.

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## SUMMARY

A review of the literature on the physiological effects of immobilization up to 1963 reveals that the effect of bedrest has been evaluated in 83 subjects (30 of whom were allowed to sit up in bed) and the effect of water immersion in 33 subjects. There is a wide variety of experimental conditions in each study which precludes any pooling of data to help evaluate the significance of some of the findings.

It is concluded that the effect of bedrest deserves further study with special attention to the following areas: 1) wider variety of subjects in regard to age, training habits, and physical condition; 2) identification of the physiological rhythms during bedrest; 3) definition of changes in body composition during recumbency; and 4) further study of the mechanism of orthostatic hypotension following bedrest.

## INTRODUCTION

Numerous studies have been conducted on the physiological effects of immobilization. The most pertinent studies, however, are those dealing with an evaluation of the effects of prolonged bedrest or water immersion in healthy subjects. Table 1 presents a chronological list of the studies published to date. The table indicates the number of subjects studied and a brief outline of the experimental design. Table 2 indicates the types of tests that were conducted in these subjects before (A), during (B), and after (C) the period of immobilization.

The information on the effects of bedrest has been compiled with that of the effects of water immersion, since both situations are analogues of the conditions prevailing of zero gravity. Knowledge gained with these two types of studies will help to evaluate more critically the changes seen during prolonged weightlessness of space flights. Although abundant physiological data have been collected already in animals and in man in the

# TABLE 1

# CHRONOLOGICAL LIST OF THE STUDIES PUBLISHED TO DATE AND EXPERIMENTAL CONDITIONS

| REF. # | YEAR | AUTHORS | SUBJECTS | PRE-IMMOBILIZATION PHASE DURATION | PRE-IMMOBILIZATION PHASE CONDITIONS | IMMOBILIZATION PHASE DURATION | IMMOBILIZATION PHASE CONDITIONS | POST-IMMOBILIZATION PHASE DURATION | POST-IMMOBILIZATION PHASE CONDITIONS |
|---|---|---|---|---|---|---|---|---|---|
| 1. | 1929 | Cuthbertson, D. | 8 | 4-5 days | "Sedentary life"<br>Performing normal functions of the ward<br>Various amounts of activity | 4-49 days | Propped up in bed<br>Movements limited<br>One leg encased in well-padded osteotomy splint with footpiece anchored<br>In some cases the other leg was attached to a sandbag<br>No massage was given | 5 days | Near normal activity |
| 2. | 1945 | Taylor, H. L.<br>Erickson, L.<br>Henschel, A.<br>Keys, A. | 6 | 42 days | Treadmill<br>Psychomotor conditioning | 21 days | Up once a day for 10 minutes<br>Bedrest | 42 days | Treadmill<br>Psychomotor conditioning |
| 3. | 1948 | Deitrick, J. E.<br>Whedon, G. D.<br>Shorr, E. | 4 | 42-56 days | Calisthenics for 1/2 hour<br>Swimming for 1/2 hour<br>Walking for 1 hour<br>(the above 4 times/week) | 42-49 days | Plaster Casts | 28-42 days | Calisthenics for 1/2 hour<br>Swimming for 1/2 hour<br>Walking for 1 hour<br>(the above 4 times/week) |
| 4. | 1948 | Spealman, C. R.<br>Bixby, E. W.<br>Wiley, J. L. | 4 | | | 24 hours | Bedrest | | |
| 5. | 1949 | Whedon, G. D.<br>Deitrick, J. E.<br>Shorr, E. | 3 | 28-38 days | Calisthenics for 1/2 hour<br>Swimming for 1/2 hour<br>Walking for 1 hour<br>(the above 4 times/week) | 35 days | Plaster Casts<br>Oscillating Bed<br>2 subjects - 8 hours/day<br>1 subject - 21 hours/day | 35 days | Calisthenics for 1/2 hour<br>Swimming for 1/2 hour<br>Walking for 1 hour<br>(the above 4 times/week) |
| 6. | 1950 | Widdowson, E.<br>McCance, R. A. | 10 | | | 3 days | Bedrest<br>No more than two pillows | 4 hours | Stood or sat on ward |
| 7. | 1961 | Graybiel, A.<br>Clark, B | 4 | 1 day | Unrestricted<br>Testing procedures | 14 days | Water immersion up to neck<br>In tanks 10 hours/day<br>In bed otherwise<br>In wheelchairs to toilet, tanks, and testing. | 3 days | Testing Procedures |
| 8. | 1961 | Graveline, D. E.<br>Balke, B.<br>McKenzie, R. E.<br>Hartman, B. | 1 | 14 days | Testing | 7 days | Water immersion up to neck<br>In tanks 23 1/2 hours/day<br>Clad in Scuba Suit | 14 days | Testing Procedures |
| 9. | 1961 | Beckman, E. L.<br>Coburn, K. R.<br>Chambers, R. M<br>DeForest, R. E.<br>Augerson, W. S.<br>Benson, V. G. | 7 | | | 12 hours (5)<br>5 hours (1)<br>23 hours (1) | Water immersion up to neck<br>Rubber suit, rubber gloves<br>Rubber hood (3) | | Testing Procedures |
| 10. | 1961 | Graveline, D. E.<br>Barnard, G. W. | 4 | 1 day | Testing: Heat<br>Centrifuge<br>Tilt<br>Psychomotor<br>Muscle strength | 6 hours<br>12 hours<br>24 hours | Complete water immersion, 18" below water surface<br>Rubber Suit<br>Partial Pressure Helmet | 1 day | Testing: Heat<br>Centrifuge<br>Tilt<br>Psychomotor<br>Muscle strength |
| 11. | 1962 | Benson, V. G.<br>Beckman, E. L.<br>Coburn, K. R.<br>Chambers, R. M. | 12 | | Testing:<br>Conditioning to centrifuge | 18 hours | Complete water immersion<br>Face masks and breathing equipment | | Testing: Centrifuge |
| 12. | 1962 | Graveline, D. E. | 5 | | Testing | 2 periods of 6 hours | SCUBA Suit with partial pressure helmet<br>With and without tourniquet protection | | Testing Procedures |
| 13. | 1962 | Browse, N. L. | 17 | 3-9 days | Control Group: 12 subjects<br>Normal Ward Routine<br>15 hours in bed<br>9 hours out of bed | 12 hours (12)<br>2 days (1)<br>3 days (2)<br>5 days (2) | Bedrest<br>Calf Blood Flow Measurement | | |
| 14. | 1963 | Brannon, E. W.<br>Potts, P<br>Rockwood, C. A. | 30 | 60 days | Control Group: 6 subjects<br>Restricted to ward<br>Given work details<br>Exercise | 60 days | Bedrest<br>Five different conditions of exercise | 10 days | Normal activity<br>Observation |
| 15. | 1963 | Birkhead, N. C.<br>Blizzard, J. J.<br>Daly, J. W.<br>Haupt, G. J. | 4 | 18 days | Testing<br>Training<br>Ergometric exercises for 30 minutes - 2 times/day | 42 days | Bedrest<br>One Pillow<br>Activity possible in recumbent position allowed | 18 days | Retraining<br>Observation<br>Ergometric exercises for 30 minutes - 2 times/day |

TABLE 2

TYPE OF TESTS CONDUCTED: (A) BEFORE, (B) DURING, (C) AFTER THE PERIOD OF IMMOBILIZATION

| References [a] | 1 | | | 2 | | | 3 | | | 4 | | | 5 | | | 6 | | | 7 | | | 8 | | | 9 | | | 10 | | | 11 | | | 12 | | | 13 | | | 14 | | | 15 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C |
| GENERAL | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| History | X | | | | | | | | | | | | | | | | | | X | | | | | | | | | | | | | | | | | | | | | | | | X | | |
| Physical | X | | | X | | | | | | | | | | | | | | | X | | | | | | | | | | | | X | | | X | | | | | | X | | | X | | |
| ANTHROPOMETRIC MEASUREMENTS | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Height | X | | X | X | | | X | | | | | | X | | | | | | | | | | | | | | | | | | | | | X | | | | | | | | | | | |
| Weight | X | X | X | X | | | X | X | X | X | | X | X | X | X | | | | X | | X | | | | X | | X | | | | | | | X | | | | | | X | X | X | X | | X |
| Circumference of Arm | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X | X | X | X |
| Circumference of Forearm | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X | X | X | X |
| Circumference of Thigh | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X | X | X | X |
| Circumference of Calf | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X | X | X | X |
| GENERAL METABOLIC | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Caloric Intake Measurements | X | X | X | X | X | X | X | X | X | | | | X | X | X | | | | | | | X | X | X | | | | | | | | | | | | | | | | X | X | X | X | X | X |
| Liquid Intake Measurements | X | X | X | | | | X | X | X | | | | X | X | X | | | | | | | X | X | X | | X | | | | | | | | | X | | | | | | | | X | X | X |
| Urine Output Measurements | X | X | X | | | | X | X | X | | | | X | X | X | | | | | | | X | X | X | X | X | | X | | X | X | | X | X | X | | | | | X | X | X | X | X | X |
| Fecal Output Measurements | X | X | X | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X |
| Basal Metabolic Rate | | | | | | | X | X | X | | | | X | X | X | | | | | | | X | | X | | | | | | | | | | | | | | | | X | X | X | X | X | X |
| Temperature | | | | | | | | | | X | X | X | | | | | | | | | | X | | X | X | X | X | | | | | | | | | | | | | | | | X | X | X |
| Food Analysis | X | X | X | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X |
| Urinalysis | X | X | X | | | | X | X | X | | | | X | X | X | | | | | | | X | | X | X | X | | | | | | | | X | X | | | | | | X | X | X | X | X |
| Fecal Analysis | X | X | X | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X |
| | | | | | | | | | | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ENDOCRINOLOGICAL | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Urinary Corticoids | | | | | | | X | X | X | | | | X | X | X | | | | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | |
| Urinary 17-ketosteroids | | | | | | | X | X | X | | | | X | X | X | | | | | | | X | X | X | | | | | | | | | | | | | | | | | | | X | X | X |
| Urinary Catecholamines | | | | | | | | | | | | | | | | | | | | | | X | X | X | | | | | | | | | | | | | | | | | | | X | X | X |
| B. E. I | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X |
| P. B. I. | | | | | | | | | | | | | | | | | | | X | | X | | | | | | | | | | | | | | | | | | | | | | | | |
| CARDIOVASCULAR | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pulse Rate | | | | X | X | X | X | X | X | X | | X | X | X | X | | | | X | | X | X | X | X | X | X | X | X | | X | | | | | | | | | | X | X | X | X | | X |
| Blood Pressure | | | | X | | X | X | X | X | X | | X | X | X | X | | | | X | | X | X | X | X | | | | X | | X | | | | X | | X | | | | X | X | X | X | | X |
| Electrocardiogram | | | | | | | X | X | X | X | | X | X | X | X | | | | X | | X | X | X | X | X | X | X | X | | X | | | | X | | X | | | | X | X | X | X | | X |
| Stroke Volume | | | | X | | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | | X |
| Cardiac Output | | | | X | | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | | X |
| Heart Size | | | | X | | X | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood Volume | | | | X | | X | X | X | X | | | | X | X | X | | | | | | | X | | X | | | | | | | | | | | | | | | | | | | | | |
| Passive Tilt Test | | | | X | | X | X | X | X | X | | X | X | X | X | | | | X | | X | X | | X | | | | X | | X | | | | X | | X | | | | | | | X | | X |
| Valsalva Maneuver | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Maximum $O_2$ Uptake | X | X | X | X | | X | X | X | X | | | | X | X | X | | | | X | | X | X | | X | | | | | | | | | | | | | | | | | | | X | | X |
| Ergometry Test (bicycle) | | | | | | | | | | X | | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | | X |
| Ergometry Test (treadmill) | | | | X | | X | | | | | | | | | | | | | X | | X | X | | X | | | | | | | | | | | | | | | | | | | | | |
| Ergometry Test (Master's) | | | | | | | X | | X | | | | X | | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ergometry Test (Schneider's) | | | | | | | X | | X | | | | X | | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heat Tolerance Test | | | | | | | | | | X | | X | | | | | | | | | | | | | | | | X | | X | | | | | | | | | | | | | | | |
| Centrifuge Test | | | | | | | | | | | | | | | | | | | | | | X | | X | X | | X | X | | X | X | X | X | | | | | | | | | | | | |
| Calf Blood Flow | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | | X | | | | | | |
| Cardiac Catheterization | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | | |
| RESPIRATORY FUNCTION | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Respiratory Rate | | | | | | X | X | X | X | | | X | X | X | X | | | | | | | X | | X | X | X | X | | | | | | | | | | | | | | | | X | | X |
| Vital Capacity | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | X | X | X | | | | | | | | | | | | | X | X | X | X | X | X |
| Timed Vital Capacity | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X |
| I. C. and E. R. V. | X | X | X | X | | X | X | X | X | | | | X | X | X | | | | X | | X | X | | X | | | | | | | | | | | | | | | | | | | X | | X |
| $O_2$ Consumption | | | | | | | | | | | | | | | | | | | | | | X | | X | X | | X | | | | | | | | | | | | | | | | X | | X |
| Chest X-ray | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X | | | |
| Basal Metabolic Rate | | | | X | X | X | X | X | X | | | | X | X | X | | | | | | | X | | X | | | | | | | | | | | | | | | | X | X | X | X | X | X |
| NEUROMUSCULAR | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Electroencephalogram | | | | | | | | | | | | | | | | | | | | | | X | | X | X | | X | | | | | | | | | | | | | | | | | | |
| General Muscle Strength | | | | X | | X | X | X | X | | | | X | X | X | | | | X | | X | | | | | | | X | | X | | | | | | | | | | X | X | X | | | |
| Biceps Strength | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | X | | X |
| Grip Strength | | | | X | | X | X | X | X | | | | X | X | X | | | | X | | X | | | | | | | X | | X | | | | | | | | | | X | X | X | | | |
| Shoulder Strength | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Arm Strength | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X | | | |
| Anterior Tibial Strength | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Gastrocnemius-soleus Strength | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Body Sway | | | | X | | X | | | | | | | | | | | | | X | | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Hand Steadiness | | | | | | | | | | | | | | | | | | | X | | X | | | | X | | X | X | | X | | | | | | | | | | | | | | | |
| Psychomotor Tests | | | | X | | X | | | | | | | | | | | | | | | | X | X | X | X | | X | X | | X | X | X | X | | | | | | | X | X | X | | | |
| PSYCHOLOGICAL TESTING | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X | | | |
| SKELETAL X-RAY | | | | | | | X | X | X | | | | X | X | X | | | | | | | | | | | | | | | | | | | | | | | | | X | X | X | | | |

[a] References are shown in Table 1

# TABLE 2 (continued)

| References | 1 | | | 2 | | | 3 | | | 4 | | | 5 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C |
| HEMATOLOGICAL TESTS | | | | | | | | | | | | | | | |
| C. B. C. | | | | | | | X | X | X | | | | X | X | X |
| Hemoglobin | | | | | | | X | X | X | X | X | X | X | X | X |
| Hematocrit | | | | X | | X | X | X | X | X | X | X | X | X | X |
| Blood Volume | | | | X | | X | X | X | X | | | | X | X | X |
| Plasma Volume | | | | X | | X | X | X | X | | | | X | X | X |
| Sedimentation Rate | | | | | | | | | | | | | | | |
| Prothrombin Time | | | | | | | X | X | X | | | | X | X | X |
| Coagulation Time | | | | | | | X | X | X | | | | X | X | X |
| Circulation Time | | | | | | | X | X | X | | | | X | X | X |
| Eosinophil Count | | | | | | | | | | | | | | | |
| Electrophoretic Pattern | | | | | | | | | | | | | | | |
| Plasma Osmolality | | | | | | | | | | | | | | | |
| BIOCHEMICAL MEASUREMENTS | | | | | | | | | | | | | | | |
| I. Blood | | | | | | | | | | | | | | | |
| Protein | | | | | | | X | X | X | X | X | X | X | X | X |
| A/G | | | | | | | | | | | | | | | |
| Na | | | | | | | X | X | X | | | | X | X | X |
| K | | | | | | | X | X | X | | | | X | X | X |
| Cl | | | | | | | | | | | | | | | |
| Bicarbonate | | | | | | | | | | | | | | | |
| $CO_2$ Combining Power | | | | | | | | | | | | | | | |
| Ca | | | | | | | X | X | X | | | | X | X | X |
| P | | | | | | | X | X | X | | | | X | X | X |
| Alkaline Phosphatase | | | | | | | | | | | | | | | |
| Glucose | | | | | | | | | | | | | | | |
| Fatty Acids | | | | | | | | | | | | | | | |
| Triglycerides | | | | | | | | | | | | | | | |
| Cholesterol | | | | | | | | | | | | | | | |
| Lactate | | | | X | | X | | | | | | | | | |
| Transaminase | | | | | | | | | | | | | | | |
| Urea | X | X | X | | | | | | | | | | | | |
| Uric Acid | X | X | X | | | | | | | | | | | | |
| Creatine | | | | | | | | | | | | | | | |
| Creatinine | | | | | | | | | | | | | | | |
| II. Urine | | | | | | | | | | | | | | | |
| Volume | | | | | | | X | X | X | | | | X | X | X |
| pH | X | X | X | | | | X | X | X | | | | X | X | X |
| Specific Gravity | | | | | | | X | X | X | | | | X | X | X |
| Albumin | | | | | | | | | | | | | | | |
| Sugar | | | | | | | | | | | | | | | |
| Acetone | | | | | | | | | | | | | | | |
| Sediment | | | | | | | | | | | | | | | |
| Na | | | | | | | X | X | X | | | | X | X | X |
| K | | | | | | | X | X | X | | | | X | X | X |
| Cl | | | | | | | | | | | | | | | |
| Ca | X | X | X | | | | X | X | X | | | | X | X | X |
| P | X | X | X | | | | X | X | X | | | | X | X | X |
| N | X | X | X | | | | X | X | X | | | | X | X | X |
| Creatinine | X | X | X | | | | X | X | X | | | | X | X | X |
| Creatine | | | | | | | X | X | X | | | | X | X | X |
| Citric Acid | | | | | | | X | X | X | | | | X | X | X |
| Sulfur | X | X | X | | | | X | X | X | | | | X | X | X |
| Magnesium | X | X | X | | | | | | | | | | | | |
| Ammonia | X | X | X | | | | | | | | | | | | |
| Urea | | | | | | | | | | | | | | | |
| Osmolality | | | | | | | | | | | | | | | |
| III. Feces | | | | | | | | | | | | | | | |
| N | X | X | X | | | | X | X | X | | | | X | X | X |
| Ca | X | X | X | | | | X | X | X | | | | X | X | X |
| P | X | X | X | | | | X | X | X | | | | X | X | X |
| Na | | | | | | | X | X | X | | | | X | X | X |
| K | | | | | | | X | X | X | | | | X | X | X |
| Sulfur | X | X | X | | | | | | | | | | | | |
| Magnesium | X | X | X | | | | | | | | | | | | |
| IV. Food | | | | | | | | | | | | | | | |
| N | X | X | X | | | | X | X | X | | | | X | X | X |
| Ca | X | X | X | | | | X | X | X | | | | X | X | X |
| P | X | X | X | | | | X | X | X | | | | X | X | X |
| Sulfur | X | X | X | | | | | | | | | | | | |
| Magnesium | X | X | X | | | | | | | | | | | | |
| Na | | | | | | | X | X | X | | | | X | X | X |
| K | | | | | | | X | X | X | | | | X | X | X |

| References | 6 | | | 7 | | | 8 | | | 9 | | | 10 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | A | B | C | A | B | C | A | B | C | A | B | C | A | B | C |
| HEMATOLOGICAL TESTS | | | | | | | | | | | | | | | |
| C. B. C. | | | | | | | X | X | X | X | | | X | | X |
| Hemoglobin | X | X | X | | | | | | | X | | | | | |
| Hematocrit | X | X | X | | | | X | X | X | X | | | X | | X |
| Blood Volume | | | | | | | X | X | X | | | | | | |
| Plasma Volume | | | | | | | | | | | | | | | |
| Sedimentation Rate | | | | | | | X | X | X | | | | | | |
| Prothrombin Time | | | | | | | | | | | | | | | |
| Coagulation Time | | | | | | | | | | | | | | | |
| Circulation Time | | | | | | | | | | | | | | | |
| Eosinophil Count | | | | X | X | X | | | | | | | | | |
| Electrophoretic Pattern | | | | | | | X | X | X | | | | | | |
| Plasma Osmolality | | | | | | | | | | | | | | | |
| BIOCHEMICAL MEASUREMENTS | | | | | | | | | | | | | | | |
| I. Blood | | | | | | | | | | | | | | | |
| Protein | X | X | X | | | | X | X | X | X | | | | | |
| A/G | | | | | | | | | | X | | | | | |
| Na | | | | | | | X | X | X | X | | | | | |
| K | | | | | | | X | X | X | X | | | | | |
| Cl | | | | | | | X | X | X | X | | | | | |
| Bicarbonate | | | | | | | | | | X | | | | | |
| $CO_2$ Combining Power | | | | | | | | | | | | | | | |
| Ca | | | | | | | X | X | X | X | | | | | |
| P | | | | | | | X | X | X | | | | | | |
| Alkaline Phosphatase | | | | | | | | | | | | | | | |
| Glucose | | | | | | | X | X | X | | | | | | |
| Fatty Acids | | | | | | | | | | | | | | | |
| Triglycerides | | | | | | | | | | | | | | | |
| Cholesterol | | | | X | | X | | | | | | | | | |
| Lactate | | | | | | | | | | | | | | | |
| Transaminase | | | | | | | X | X | X | | | | | | |
| Urea | | | | | | | X | X | X | | | | | | |
| Uric Acid | | | | | | | | | | | | | | | |
| Creatine | | | | | | | | | | | | | | | |
| Creatinine | | | | | | | | | | | | | | | |
| II. Urine | | | | | | | | | | | | | | | |
| Volume | | | | | | | | | | X | X | | X | | X |
| pH | | | | | | | | | | X | X | | | | |
| Specific Gravity | | | | | | | | | | X | X | | X | | X |
| Albumin | | | | | | | | | | | | | | | |
| Sugar | | | | | | | | | | | | | | | |
| Acetone | | | | | | | | | | | | | | | |
| Sediment | | | | | | | | | | | | | | | |
| Na | | | | | | | X | X | X | X | X | | | | |
| K | | | | | | | X | X | X | X | X | | | | |
| Cl | | | | | | | X | X | X | X | X | | | | |
| Ca | | | | | | | X | X | X | X | X | | | | |
| P | | | | | | | X | X | X | | | | | | |
| N | | | | | | | X | X | X | X | X | | | | |
| Creatinine | | | | | | | | | | | | | | | |
| Creatine | | | | | | | | | | | | | | | |
| Citric Acid | | | | | | | | | | | | | | | |
| Sulfur | | | | | | | | | | | | | | | |
| Magnesium | | | | | | | | | | | | | | | |
| Ammonia | | | | | | | | | | | | | | | |
| Urea | | | | | | | | | | | | | | | |
| Osmolality | | | | | | | | | | | | | | | |
| III. Feces | | | | | | | | | | | | | | | |
| N | | | | | | | | | | | | | | | |
| Ca | | | | | | | | | | | | | | | |
| P | | | | | | | | | | | | | | | |
| Na | | | | | | | | | | | | | | | |
| K | | | | | | | | | | | | | | | |
| Sulfur | | | | | | | | | | | | | | | |
| Magnesium | | | | | | | | | | | | | | | |
| IV. Food | | | | | | | | | | | | | | | |
| N | | | | | | | | | | | | | | | |
| Ca | | | | | | | | | | | | | | | |
| P | | | | | | | | | | | | | | | |
| Sulfur | | | | | | | | | | | | | | | |
| Magnesium | | | | | | | | | | | | | | | |
| Na | | | | | | | | | | | | | | | |
| K | | | | | | | | | | | | | | | |

| References | 11 | | | 12 | | | 13 | | | 14 | | | 15 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | A | F | C | A | B | C | A | B | C | A | B | C | A | B | C |
| HEMATOLOGICAL TESTS | | | | | | | | | | | | | | | |
| C. B. C. | | | | | | | | | | X | X | X | X | | |
| Hemoglobin | | | | | | | | | | X | X | X | X | X | X |
| Hematocrit | | | | X | X | X | | | | X | X | X | X | X | X |
| Blood Volume | | | | | | | | | | | | | | | |
| Plasma Volume | | | | | | | | | | | | | | | |
| Sedimentation Rate | | | | | | | | | | X | X | X | | | |
| Prothrombin Time | | | | | | | | | | X | X | X | | | |
| Coagulation Time | | | | | | | | | | | | | | | |
| Circulation Time | | | | | | | | | | | | | | | |
| Eosinophil Count | | | | | | | | | | | | | | | |
| Electrophoretic Pattern | | | | | | | | | | X | X | X | | | |
| Plasma Osmolality | | | | X | X | | | | | | | | | | |
| BIOCHEMICAL MEASUREMENTS | | | | | | | | | | | | | | | |
| I. Blood | | | | | | | | | | | | | | | |
| Protein | | | | | | | | | | X | X | X | X | X | X |
| A/G | | | | | | | | | | X | X | X | X | X | X |
| Na | | | | X | | X | | | | X | X | X | X | X | X |
| K | | | | X | | X | | | | X | X | X | X | X | X |
| Cl | | | | | | | | | | X | X | X | X | X | X |
| Bicarbonate | | | | | | | | | | | | | | | |
| $CO_2$ Combining Power | | | | | | | | | | | | | X | X | X |
| Ca | | | | | | | | | | X | X | X | X | X | X |
| P | | | | | | | | | | X | X | X | X | X | X |
| Alkaline Phosphatase | | | | | | | | | | X | X | X | X | X | X |
| Glucose | | | | | | | | | | X | X | X | X | X | X |
| Fatty Acids | | | | | | | | | | | | | X | X | X |
| Triglycerides | | | | | | | | | | | | | X | X | X |
| Cholesterol | | | | | | | | | | X | X | X | X | X | X |
| Lactate | | | | | | | | | | | | | X | | X |
| Transaminase | | | | | | | | | | | | | | | |
| Urea | | | | X | | X | | | | | | | | | |
| Uric Acid | | | | | | | | | | | | | | | |
| Creatine | | | | | | | | | | X | X | X | | | |
| Creatinine | | | | | | | | | | X | X | X | | | |
| II. Urine | | | | | | | | | | | | | | | |
| Volume | X | | X | X | X | X | | | | | | | | | |
| pH | | | | | | | | | | X | X | X | X | X | X |
| Specific Gravity | X | | X | X | X | X | | | | X | X | X | | | |
| Albumin | | | | | | | | | | | | | X | X | X |
| Sugar | | | | | | | | | | | | | X | X | X |
| Acetone | | | | | | | | | | | | | X | X | X |
| Sediment | | | | | | | | | | | | | X | X | X |
| Na | | | | X | | X | | | | X | X | X | | | |
| K | | | | X | | X | | | | X | X | X | | | |
| Cl | | | | | | | | | | X | X | X | | | |
| Ca | | | | | | | | | | X | X | X | X | X | X |
| P | | | | | | | | | | | | | X | X | X |
| N | | | | | | | | | | | | | X | X | X |
| Creatinine | | | | X | | X | | | | X | X | X | X | X | X |
| Creatine | | | | | | | | | | X | X | X | | | |
| Citric Acid | | | | | | | | | | | | | | | |
| Sulfur | | | | | | | | | | | | | | | |
| Magnesium | | | | | | | | | | | | | | | |
| Ammonia | | | | | | | | | | | | | | | |
| Urea | | | | X | X | | | | | | | | | | |
| Osmolality | | | | X | X | | | | | | | | | | |
| III. Feces | | | | | | | | | | | | | | | |
| N | | | | | | | | | | | | | X | X | X |
| Ca | | | | | | | | | | | | | | | |
| P | | | | | | | | | | | | | | | |
| Na | | | | | | | | | | | | | | | |
| K | | | | | | | | | | | | | | | |
| Sulfur | | | | | | | | | | | | | | | |
| Magnesium | | | | | | | | | | | | | | | |
| IV. Food | | | | | | | | | | | | | | | |
| N | | | | | | | | | | | | | X | X | X |
| Ca | | | | | | | | | | | | | X | X | X |
| P | | | | | | | | | | | | | | | |
| Sulfur | | | | | | | | | | | | | | | |
| Magnesium | | | | | | | | | | | | | | | |
| Na | | | | | | | | | | | | | | | |
| K | | | | | | | | | | | | | | | |

course of orbital flights, their interpretation is difficult because of restriction of measurements, lack of experimental control, and limitation of the number of subjects who can be studied under these experimental circumstances. Therefore, no attempt has been made here to review the significance of the studies reported.

## COMMENTS ON PUBLISHED STUDIES

Cuthbertson[1] conducted one of the first studies of the effects of prolonged bedrest in healthy human subjects in 1929. He kept eight subjects (six men and two women) on bedrest for periods ranging from 9 to 12 days. His observations, mainly metabolic, included a loss of sulphur, nitrogen, phosphorus and calcium (to a lesser degree) during bedrest. He did not comment on the increased urinary output of the subjects during bedrest, but he reported the values of 24-hour urine in three of his experiments. These values indicate a significant increase in urinary output, especially at the beginning of bedrest. The metabolic changes were more profound at the initial stages of bedrest and they seemed to level off as bedrest continues. This was especially evident in calcium losses. He attributed the losses of metabolic products to the decreased activity of the musculoskeletal system and stated clearly the need for studies of longer duration to obtain clear cut trends of the changes observed.

The study of Taylor, Erickson, Henschel, and Keys[2] was reported first in 1945.

Additional information was reported in a second publication by Taylor, Henschel, Brozek, and Keys[3] in 1949. Six healthy subjects were studied during a period of physical conditioning (by means of various types of exercise) before they were placed on bedrest for three weeks (four subjects) or for four weeks (two subjects). Following bedrest the subjects underwent a six-week period of physical reconditioning. The conditions of bedrest were not strict since each individual could be up and about for 10 minutes every day in order to perform emunctory functions. This may have prevented a greater deterioration of the cardiovascular adaptation to postural changes. Following the period of bedrest, all the individuals had a decreased tolerance to passive tilt as judged from the changes in pulse pressure and heart rate, but none of the subjects fainted during tilt. The passive tilt was carried out for 15 minutes with a foot board to support the weight of the body. Observations on the cardiovascular system include a significant decrease of the end systolic volume of the heart at the end of bedrest, as measured by a roentgenographic technique. There was an increase of the resting heart rate (by 0.41 beats per day in the morning pulse rate and by 0.67 beats per day in the evening pulse rate). These observations suggest an increase in sympathetic tone as a result of bedrest. Indeed an adrenergic reaction could account for the increase in the cardiac frequency and for a more forceful contractility of the myocardium (inotropic effect) which would result in more complete emptying of the ventricle with each stroke. However, an absolute increase in stroke volume may not have occurred if the venous return was significantly impaired at the end of bedrest. The "deconditioning" of the cardiovascular system was manifested also by an increase in the heart rate during exercise after bedrest. This response persisted for more than 16 days after bedrest. It is unfortunate that measurements of blood pressure and heart rate were carried out only at the steady state of passive tilt, for no data are available on the dynamic changes in these variables in the course of the tilt maneuver. The changes produced by passive tilt could be elicited still 49 days following bedrest, but they were not detectable 72 days after bedrest. One of the subjects was evaluated also for a second period of bedrest following a herniorrhaphy. It is interesting that no significant difference was noted in the "deconditioning" of the cardiovascular system of this individual between the period of voluntary bedrest and the post-operative confinement.

The study of Deitrick, Whedon, and Shorr[4] is a classic in the literature of the effects of bedrest. The study was conducted in four healthy young men for a period of six weeks (two subjects) and seven weeks (two subjects). These subjects did calisthenics, swam, and walked for a period of control of six to eight weeks. During bedrest the individuals were placed in bivalve casts that extended from the umbilicus to the toes. The subjects were removed from the casts daily for hygiene purposes and for ergometer and tilt table tests. The rest conditions were more rigorous than in other studies, but it is likely that the placement of the subjects in the body cast presented an added stress. The subjects of this study also exhibited marked deterioration of their tolerance to tilt. The tilts were conducted with the feet supported by a foot board and the subjects remained in the tilt posture for 10 or 20 minutes unless fainting occurred in a shorter interval. Compared to pre-immobilization measurements, there was a decline of the total blood volume and a marked decrease in the exercise tolerance after immobilization as measured by Master and Schneider tests which showed the individual had an increase in the resting pulse rate and in the heart rate response to exercise. There was recovery of most of the physiological functions three to four weeks following the bedrest although the exercise tolerance was not recovered until six weeks. Their study failed to show any decrease in the heart size; but Taylor[2,3], in interpreting the data of Deitrick[4] indicates that the technique used by the latter authors probably was not accurate to measure the changes in the cardiac size. The daily testing of the subjects for ergometry and tilt tolerance increased the knowledge on the natural history of the effects of immobilization, but it is possible that this had a protective effect in preventing more venous "deconditioning" and fluid shifts from the extravascular compartment which would have occurred if the subject had remained horizontal 24 hours every day. There is a discrepancy between the weight changes in the study of Taylor[2,3] and in that of Deitrick.[4] Whereas Taylor observed a significant decrease in weight during the period of bedrest, Deitrick did not observe a significant change. However, as Taylor points out, the caloric intake of subjects in the study of Deitrick was somewhat excessive for the metabolic demands imposed during the stay in bed. The metabolic measurements by Deitrick indicate an increased nitrogen excretion which began on the fifth or sixth day of immobilization and reached its peak during the first half of the second week. There was an increased urinary and fecal excretion of calcium which reached a maximum by the fourth or fifth week with a slight elevation in serum calcium at the end of the immobilization period. There was no appreciable increase in urinary output during the bedrest period, but in a subsequent report it was indicated that the volume of urine increased by 205 cc. during immobilization. There was an increase in the excretion of phosphorus, total sulphur, sodium, and potassium during bedrest. There was a lowering of the creatinine tolerance during immobilization and a significant decrease in muscle mass and muscle strength of the immobilized limbs. The results of the study of the 17-ketosteroid excretion were contradictory, and only one subject showed a significant lowering of this excretion.

Spealman, Bixby, Wiley, and Newton[5] evaluated the effect of bedrest on four subjects for 20 hours. They reported a decreased tolerance to tilt and to ergometry tests following bedrest. These effects were more marked when rest was attained in a cold environment. They reported also an increase in concentration of hemoglobin following bedrest although the total circulating blood decreased by five per cent. The experimental design of Spealman's study included testing of subjects under different environmental conditions before bedrest, and the data published do not permit establishing conclusively that the subjects' conditions at the start of bedrest were comparative to those at the onset of all the experiments. The changes in rate during tilt may not be significant, and unfortunately the values of blood pressure were not published. Although he attributed "deconditioning" to a decrease in blood volume, the supporting data are not sufficient to warrant this conclusion.

In a second study, Whedon, Deitrick, and Shorr[6] evaluated the effect of an oscillating bed in preventing the physical "deconditioning" produced by immobilization. The conclusion of the experiment was that intermittent periods of oscillation diminished considerably the metabolic and physiological effects of bedrest. A better tolerance to tilt and a lesser degree of excretion of nitrogen, calcium, and phosphorus were accomplished. The study was conducted in three healthy subjects who had participated in the study of bedrest without an oscillating bed. They do not give data pertaining to urinary output, but the authors state that the urine volume increased slightly by an average of 250 cc. daily; it was higher during the immobilization periods than during the control periods.

Widdowson and McCance[7] studied the effect of bedrest over a period of 67 hours on 10 hospital patients with various impairments which according to the authors were not expected to produce any significant changes in blood volume distribution. This assumption may not be valid since information is not available on the specific type of impairments, on their clinical condition at the time of the study, and on the medications the patients were receiving. In these 10 subjects there was a drop in the hemoglobin and hematocrit at the initial period of bedrest. This was followed by an increase in the hemoglobin and hematocrit which they attributed to a decrease in the plasma volume.

A water load given to these subjects at the end of bedrest produced a normal diuretic effect which would not be expected if the plasma volume had been low. The results are difficult to interpret since no other data are available in regard to blood volume, urinary output, etc.

The study of Graybiel and Clark[8] is the first of a series of studies of the effects of prolonged water immersion. They evaluated the effect of water immersion for a period of four hours and two subsequent periods of three hours each, every day for two weeks. When the subjects were out of the water, they remained in bed and they used a wheel chair for transfer to the toilet and for transportation to and from the tank of water. Tilt studies (with foot board) were done throughout the experimental period. There was a drop in diastolic blood pressure as the number of periods of water immersion increased in the course of the experiment. Postural hypotension developed rapidly and approximately four hours of immersion were sufficient to bring this effect out following the completion of the experiment. Four days were needed for the subjects to recover their ability to tolerate passive tilt without any abnormal changes in heart rate or blood pressure. Throughout the period of study, the individuals slept well but described a feeling of weakness. Their muscular strength was unchanged, but they had a decreased exercise tolerance. The authors describe the physiological status resulting from water immersion as due to a "zero G asthenia".

Graveline and co-workers[9] conducted a series of experiments to evaluate the effect of water immersion. The initial study was conducted by Graveline, Balke, McKenzie, and Hartman on Graveline himself. He remained in a specially built tank for seven days totally underwater except for his head. He emerged once a day for hygiene purposes. The results of this study revealed that he exhibited rapidly a sense of fatigue and a marked decrease in the tolerance to tilt. He also showed a decrease in pulse pressure and an increase in diastolic blood pressure at the time of tilt. Throughout the period of bedrest, his white blood count and hematocrit increased, the plasma globulins increased, and the albumin/globulin ratio decreased. He had a large output of urine with a large output of nitrogen and electrolytes, but this effect of nitrogen urine elimination leveled off later on. His tolerance to positive G acceleration decreased very markedly as manifested by an increase in the heart rate in response to the accelerative forces. Throughout the period of immersion he exhibited a drop in the blood pressure with essentially unchanged pulse pressure. The electrocardiogram revealed a decrease of the amplitude of the T waves. There was an initial increase in his output of catecholamines which later returned to normal. His plasma corticoids were increased but the urinary corticoids remained normal throughout the experiment.

Beckman, Coburn, Chambers, DeForest, Augerson, and Benson[10] reported on the results of a study of the effect of water immersion on one subject for five hours. No appreciable change was noted in this individual's tolerance to passive tilt or other tests of physiological competence. On one other subject who was immersed for 23 hours, there was a diuresis and decreased specific gravity of the urine. The subject exhibited atrial tachycardia and syncope upon sitting after coming out of the water. Later he had an episode of paroxysmal tachycardia which reversed spontaneously. This subject had marked weight loss. In addition, five subjects were studied for a period of 12 hours and these individuals had marked polyuria and decreased specific gravity with weight loss within a half of an hour. Their respiratory rate also increased. There was a marked increase in serum phosphorus and a decrease in the albumin/globulin ratio as demonstrated by electrophoresis but increase in albumin/globulin ratio when albumin and globulins were measured with precipitation technique. The tolerance of these individuals' positive acceleration decreased very markedly. Their studies of lung compartments showed that during water immersion there was a marked change in the expiratory reserve volume which decreased by 64 per cent while the inspiratory capacity increased by 32 per cent. The over-all effect in vital capacity was negligible. Although the functional residual capacity was not measured, it is logical to assume that it decreased markedly.

Graveline and Barnard [11] reported on studies conducted in four subjects who were submitted to periods of immersion of 6, 12, and 24 hours. Passive tilt after each of these periods caused a marked increase in heart rate and a decrease in pulse pressure which had a negative and steep slope. The systolic blood pressure also had a negative and steep slope, but the diastolic pressure remained constant, the values being higher than at $0^{o}$. These individuals exhibited also lower tolerance to positive acceleration and to environmental heat. When these individuals were submitted to water immersion for six hours, they showed evidence of hemodilution, but if they remained under water for twenty-four hours they had hemoconcentration.

The study of Benson, Beckman, Coburn, and Chambers [12] was conducted by 12 subjects who were professional skin divers. They were under water but wore helmets that permitted them to breathe against a positive pressure. They were subjected to a training period of positive acceleration before water immersion. After 18 hours of water immersion with positive pressure breathing, these individuals showed a slight decrease of the tolerance to positive acceleration. It is interesting that these individuals did not have water diuresis nor a decrease in specific gravity of the urine. These results are in contrast with those of Graveline [9] who even in those individuals immersed in water and breathing under positive pressure was able to demonstrate a marked water diuresis and hyposthenuria.

In a subsequent study, Graveline [13] evaluated the effect of six hours of water immersion on five subjects who were immersed in water with helmets to provide for pressure regulation and to decrease the "negative pressure breathing" effects of water immersion with the head out. In these individuals he conducted cardiovascular and metabolic studies, the results of which were reported separately. Graveline demonstrated the protective effect of intermittent inflation of tourniquets in the extremities. The same individuals who had exhibited postural hypotension during water immersion without toruniquets had good tolerance to tilt after an identical period of time of water immersion with tourniquets. The metabolic study of Graveline and Jackson [14] was aimed to document the phenomenon of diuresis resulting from water immersion and to study its mechanisms. After initial hemodilution they showed an increase in the hematocrit of the blood of these individuals during immersion. The measurement of hematocrit was done upon emersion from the water. There was a decrease in the osmolality of the urine and polyuria. This effect of water immersion was attributed to an inhibition of antidiuretic hormone and aldosterone, secondary to the increased circulating blood volume which occurs during recumbency or during water immersion. A cardiovascular study conducted in these subjects showed that they had marked decrease in their tolerance to passive tilt. This was manifested by an increase in heart rate and a decrease in the systolic blood pressure and in pulse pressure in spite of a marked increase in diastolic blood pressure. The slope of the diastolic blood pressure during tilt was flat or slightly positive on almost all the subjects of Graveline's studies [13] with the exception of two subjects who had a negative slope before they exhibited syncope.

The study of Browse [15] was conducted in 12 hospital subjects (presenting minor impairments) who remained in bed for 12 hours and in 5 subjects who remained in bed for periods ranging from two to five days. His study was limited to evaluate the degree of blood flow through the calf, and the results of his study failed to reveal any significant change in the amount of flow through the inactive extremities. He reached the conclusion that bone demineralization and loss of muscle mass occurring during rest are not the result of a decreased blood flow to the inactive extremities.

Brannon, Rockwood, and Potts [16] reported on a method for evaluating the effect of bedrest on 30 subjects who were confined to bed for a period of 60 days. The study was oriented mainly to determine the effect of inactivity on the weight bearing joints, skeletal demineralization, and muscular "deconditioning". They established five groups of six subjects each; each group being submitted to a different regime of bedrest with different types of isotonic or isometric exercises. The subjects were allowed to sit up in bed during the study. Although several metabolic and cardiovascular tests were conducted on these subjects, the results are not available. They indicated, however, that these subjects had loss of muscular mass in the legs which could have been loss of fluid and that those who were submitted to rest without exercise had dizziness, unsteady gait, low back pain, and fatigability when normal activities were resumed. They failed to show any calcium depletion, and no X-ray changes were noted by the clinical method that they used to evaluate this particular aspect of bone. They indicated that the isometric exercises were useful in preventing some of the symptomatology of the individuals.

They concluded that a small amount of exercise is sufficient to prevent loss of muscle mass and bone demineralization.

Birkhead, Blizzard, Daly, Haupt, Issekutz, Myers, and Rodahl[17] studied the effect of bedrest in four healthy men. These subjects remained under observation for three weeks and they spent 18 days on a program of physical exercise for training. Then they were submitted to 40 days of rest followed by 18 days of observation and physical retraining. The immobilization was not complete since the individuals were allowed to move their legs and arms while in bed; but they remained horizontal at all times even for feeding and for emunctory functions. The cardiovascular and metabolic results of this study must be interpreted in the light of the experimental conditions under which the study was conducted. The period of physical conditioning had physiological effects on the subjects. From a theoretical standpoint the effects were opposite to those of bedrest and to some extent the initial impact of bedrest on these individuals was minimized because of their physical condition at the time that the rest began. It is difficult to establish an assessment of the effect of bedrest on the cardiovascular system because most of the tests before rest were obtained during cardiac catheterization which could not be repeated following the bedrest. It is likely that the stress of the cardiac catheterization yielded cardiac dynamic values that are not typical of the response of the healthy subjects to passive tilt since two of the individuals had hypotension even before they were subjected to bedrest. After bedrest three subjects developed hypotension and the fourth subject had to be excluded because of a severe cardiovascular disturbance when cardiac catheterization was attempted. The results of blood pressure changes in the course of tilt are not available. The subjects were supported with a foot board during tilt. The authors' data appear conclusive on the effect of bedrest on the cardiovascular response to exercise. Their subjects had a higher cardiac output during exercise after bedrest. This was due to an increase in heart rate and in stroke volume, but the latter did not occur at high work loads probably as a result of tachycardia. The subjects required about 18 days to recover the control heart rate. Their metabolic results on creatinine, nitrogen, calcium, phosphorus excretions, 17-ketosteroids, and catecholamine excretions are difficult to interpret because the urines of each subject were pooled over a six-day period of time. There were no studies of the mineral losses through the stools. An unusually high calcium content (1734 mg.) diet was used. In this study it is reported that there was an increase in urinary output of nitrogen, calcium, and phosphorus but no significant change in catecholamines or in serum creatinine excretion. The ketosteroid values were slightly higher following bedrest, but it is questionable that this had any statistical significance.

## CONCLUSION

Although the number of studies of the effect of bedrest and water immersion have been abundant, the volume of information available is not commensurate to the efforts made hereto.

In all, the effect of bedrest has been evaluated in 83 subjects (30 of whom were allowed to sit up in bed) and the effect of water immersion in 33 subjects.

There is a wide variety of experimental conditions in each study which precludes any pooling of data to help evaluate the significance of some of the findings.

If one accepts that the effect of bedrest deserves further study, the following areas of investigation require special attention:

1. The effect of bedrest must be quantified on a wider variety of healthy subjects of different age, occupation, physical training habits, and physiological condition.

2. Greater emphasis must be made on evaluating the dynamic characteristics of the physiological and metabolic changes occurring throughout the period of immobilization. There must be an identification of the fluctuations and rhythms in the behavior of the physiological systems.

3. There is a need to define further the changes in the body composition and fluid shifts occurring during recumbency, and these changes must be evaluated serially.

4. There is a need to document the fluctuations in cardiac dynamics during bedrest. Indirect methods for assessing cardiac dynamics should be preferred over current techniques, for they would permit the evaluation of the subject with minimum disturbance.

5. There is a need to delineate further the mechanism of orthostatic hypotension resulting from bedrest and to study the dynamic changes in the circulatory and neuroregulatory centers during passive tilt. A biocybernetic approach to the study of the cardiovascular responses may contribute greatly to this evaluation.

6. The neuroendocrine responses to prolonged immobilization must be likewise studied in a dynamic fashion. It is important to determine the role played by the hypothalamic - pituitary - adrenal axis under these conditions.

7. Finally, it would be useful to consider the possible differences in time constants of changes in the neural, hormonal, and metabolic controls of the physiological changes occurring during bedrest.

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